REMARKS

Claims 1-6, 8-10, and 15-19 are pending in this application. Applicants request that the following amendments be entered. Withdrawn claims 7 and 11-14 have been canceled without prejudice or disclaimer. Applicants have amended claims 1-4. Support for the amendment to claim 1 can be found in the specification, for example, on page 8, lines 6-9. The amendments to claims 2-4 correct the claim dependencies. No new matter has been added by the amendments.

Applicants have not canceled claim 8 because Applicants intend to rejoin claim 8 once the composition claim from which it depends is deemed allowable.

Information Disclosure Statement

The Information Disclosure Statement filed on March 17, 2005 was not considered by the Examiner because the citation therein was allegedly an incomplete citation. Applicants submit herewith a substitute Form PTO-1449 in which the author, accession number, and date on which the reference was created are listed. The reference is an EMBL sequence entry and the date on which the reference was created is presumably the date on which the reference was first publicly available, as the EMBL creation date and the date on which this same sequence entry was first publicly available on the NCBI database are the same. A copy of the listed reference is also provided. As this reference has previously been cited, Applicants request its consideration by the Examiner. It is believed that no fees are due for this substitute Form PTO-1449.

Claim Objections

The Office Action objected to claims 2-4 as improperly depending from only a part of claim 1. Applicants have amended claims 2-4 to depend from claim 1, as suggested by the Examiner, and use the newly added language to indicate that they do not cover any part of claim 1 other than part (c).

35 U.S.C. § 101 and § 112, First Paragraph

The Office Action maintains the rejection of claims 1-6, 9, 10, and 15-19 as allegedly lacking utility. Applicants reiterate the arguments presented in the Reply to Office Action filed on July 5, 2005, and submit the following additional arguments.

Asserted Utility

The asserted utility of the claimed DEC2 nucleic acids and proteins stems in part from their role as bHLH transcription factors and their significant homology to members of the DEC1 subfamily, including DEC1 and SHARP-1. As such, they find utility in controlling cell development and differentiation, as markers of development and differentiation, and as targets in the development of pharmaceutical agents for disorders, such as osteoarthritis, associated with the proteins of the present invention (see, e.g., page 3, lines 25-30). For example, as described in the specification, DEC2 is important in elucidating the differentiation and deformation mechanisms of cartilage and therefore is expected to be useful in developing therapies for the treatment of osteoarthritis, rheumatoid arthritis, etc. (page 5, lines 7-22).

Further, the DEC2 proteins have utility because they are members of the DEC1 subfamily of bHLH transcription factors, which has a well-established utility. Evidence of structural similarity to a compound known to have a particular therapeutic or pharmacological utility supports an assertion of therapeutic utility for the new compound (MPEP § 2107.03(II)). In this case, DEC1, Stra13, and SHARP-1 all have a well-established utility as regulators of differentiation. This uncontested fact is established both by the originally-filed specification and the Azmi reference (*J. Biol. Chem.* **279**:52643-53652 (2004)) submitted with the previous response. As described on page 3, lines 15-16, of the application, the DEC2 proteins of the instant invention share 90% or greater identity with the DEC1 and SHARP-1 proteins in the conserved bHLH region (i.e., the region that dictates activity, e.g., regulation of differentiation). Accordingly, as newly identified members of the DEC1 subfamily of bHLH transcription factors that possess 90% or greater identity in the region that dictates protein activity, it is reasonable to presume that the DEC2 proteins share this well-established utility as regulators of tissue differentiation.

An Assertion of Utility Creates a Presumption of Utility

An assertion of utility creates a presumption of utility that is generally sufficient to satisfy the utility requirements of 35 U.S.C. § 101. As stated in *In re Langer* (503 F.2d 1380, 1391 (CCPA 1974)):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope. (emphasis in the original)

The Office Action (at page 12) states that it has made no argument alleging a lack of credibility for the asserted use. Thus, by accepting the credibility of Applicants' asserted utility, the Examiner implicitly admits that there is no reason to question the objective truth of Applicants' statement of utility or its scope. Further, the Office Action has failed to offer any evidence in support of its allegation that a skilled artisan would question the objective truth of the statement of utility. Accordingly, the specification satisfies the utility requirement of 35 U.S.C. § 101.

The Analysis Set Forth in the Utility Guidelines Supports a Finding of Utility

The Office Action alleges that the claims lack a credible, specific, and substantial utility. In support of this allegation, the Office Action recites (at pages 6-8) five examples of asserted utilities found in the specification and the purported deficiencies of each. Applicants do not agree that these asserted utilities are inadequate, and further note that the Office Action fails to address other utilities asserted in the specification, not cited by the Office Action, each of which also is credible, specific, and substantial. For example, as stated at page 5, lines 7-8 (emphasis added), "The present invention provides novel bHLH type transcription factors and DNA encoding the proteins," and at lines 20-21, "For example, 'DEC2' is important in elucidating the differentiation and deformation mechanisms of cartilages ..."

According to the standards set forth in the U.S. Patent and Trademark Office's Revised Interim Utility Guidelines Training Materials of 1999 ("Utility Guidelines"), the asserted utilities amply suffice to meet the statutory utility requirement. First, the asserted utilities are specific. According to the Utility Guidelines, a utility is "specific" in the sense that it "contrasts with a

general utility that would be applicable to the broad class of the invention" (page 5). The broad class of the invention here is nucleic acids. Unlike other members of this broad class, the specific nucleic acids recited in the claims encode proteins that have specific bHLH domains and function specifically as DEC1 subfamily bHLH transcription factors. Not all nucleic acids encode proteins that function as transcription factors, not to mention function as bHLH transcription factors of the DEC1 subfamily. Thus, the asserted utilities are specific.

The Office Action states at page 9 that:

> [U]nlike ligases in which the enzymatic activity is defined and can be clearly used by any protein having that activity because a ligase has a specific, substantial, and credible utility, even though bHLH transcription factors have related structures, they have very different specific activities because each family member regulates the expression of different genes which then affect different cellular processes (e.g., myogenesis, neurogenesis, and hematopoiesis). Each family member does not have all of these activities, but instead has specific activities that are very different from the other family members. So, unlike ligase, once a member of the bHLH transcription factor is identified, one would not know what specific activity it has in the absence of empirically determined data. (emphasis added)

The Office Action notes that once a protein is identified as a "ligase," its utility is clear and that all ligases have the same "ligase" activity. Applicants agree and point out that the standards set for in the Utility Guidelines (e.g., Example 10) do not require a high level of precision in identifying a protein's function. Indeed, as Example 10 itself demonstrates, identification of a protein as being merely a "ligase" is sufficient to confer utility. The term "ligase" is actually broad, and all ligases do not possess the same precise function. For example, a ligase can be a DNA ligase, an RNA ligase, or a protein ligase (e.g., ubiquitin-protein ligase), each of which has distinct substrate specificity. Yet according to the Utility Guidelines, mere identification of a generic "ligase" function is sufficient to satisfy the utility requirement. Likewise, determination that a nucleic acid encodes a transcription factor also satisfies this prong of the utility standard. Not only does the application disclose that the nucleic acids recited in the claims encode a specific type of transcription factor, namely, a bHLH type transcription factor, the application further discloses that the nucleic acids encode transcription factors of the DEC1 subfamily, which is more than adequate to satisfy the "specific utility" requirement set forth in the Utility Guidelines.

Next, the asserted utilities are "substantial." According to the Utility Guidelines, a utility is substantial if it defines a "real world" use (page 6). The claimed nucleic acids encode proteins that have a real world use, for example, use in elucidating differentiation and deformation mechanisms of cartilage, as described above.

The Office Action states at pages 11-12 that:

> The applicants argue that the asserted utility is a substantial utility because it defines a real world use: the protein is expected to control development and tissue differentiation, and given their role in differentiation of cartilaginous tissues, they can be used for screening for substances in treating conditions such as osteoarthritis. This argument is not persuasive because controlling development and tissue differentiation is too generic of a utility to be used in the absence of the identification of which specific cells are affected (and how they are affected) during development and what tissues (and how the tissues are) affected during differentiation. In order to determine and confirm the specific real world use of the claimed protein, one would have to conduct significant further experimentation to identify and confirm which cells and tissues are affected (and how they are affected) during development and tissue differentiation. Therefore, the asserted utility is not substantial.

As described above, the proteins encoded by the claimed nucleic acids likely play a role in the differentiation of cartilage and can be used to elucidate differentiation and deformation mechanisms of cartilage; thus, the specific tissue type in which these proteins function is identified. As a result, "significant further experimentation" does not need to be performed "to identify and confirm which cells and tissues are affected." Furthermore, as acknowledged by the above-quoted passage, Applicants have explained that the protein can be used in screening substances to be used for treating conditions such as osteoarthritis. It is incontrovertible that screening for substances to be used in treating osteoarthritis qualifies as "substantial." See the Utility Guidelines at page 6: "Both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a 'substantial utility' define a 'real world' context of use." As osteoarthritis is a known disease, treating it is a substantial utility, and assaying for compounds that can treat it is a substantial utility. If the Examiner believes that more work needs to be done to prove that the claimed nucleic acids can be used for that purpose, that goes to the credibility of the utility, not whether

utility is "substantial." The Examiner in fact does not directly challenge the credibility of the asserted utilities, probably because it is clear that they meet the credibility standard.

The Utility Guidelines state on page 5 that "[a]n assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion." The Office Action (at page 12) states that it has made no argument alleging a lack of credibility for the asserted use. Thus, this prong of the three-prong test for utility is also satisfied.

Current Federal Circuit Case Law Supports a Finding of Utility

The Federal Circuit's recent holding in *In re Fisher* (421 F.3d 1365 (Fed. Cir. 2005)) also supports a finding of utility in the present case. With respect to the requirement that the asserted utility be specific, the court stated:

> Turning to the "specific" utility requirement, an application must disclose a use which is not so vague as to be meaningless. Indeed, one of our predecessor courts has observed "that the nebulous expressions 'biological activity' or 'biological properties' appearing in the specification convey no more explicit indication of the usefulness of the compounds and how to use them than did the equally obscure expression 'useful for technical and pharmaceutical purposes'"... Thus, in addition to providing a 'substantial' utility, an asserted use must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public. (*Id.* at 1371; emphasis added).

In stark contrast to the situation in *Fisher*, Applicants have provided a full-length sequence and have asserted utilities that are specific to proteins of similar sequence– a far cry from the generic utilities posited in the *Fisher* application. The presently asserted utilities would have significant and presently available benefit to the public. Clearly, therefore, they meet the standards laid down in *Fisher*.

As discussed above, the Office Action did not question the credibility of the asserted utility (Office Action at page 12). Thus, the three-prong utility test set forth by current case law is satisfied by the present application.

Applicants have demonstrated that a specific, substantial, and credible utility exists for the invention described herein. Further, the invention satisfies the utility requirements as set forth by both the Utility Guidelines and recent case law from the Federal Circuit. Thus, for the nucleic acids recited in the pending claims, the utility requirement of 35 U.S.C. § 101, and that of 35 U.S.C. § 112, first paragraph, is satisfied.

CONCLUSION

Applicants respectfully submit that the rejections of claims 1-6, 9, 10, and 15-19 have been overcome by the arguments presented herein and that all claims are in condition for allowance.

Apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 14875-101001.

Respectfully submitted,

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